REMARKS

These remarks are in response to the Office Action dated April 24,2006. Applicants have amended claims 1, 2, 3, 4 and 24. Support for the amendments can be found throughout the specification and claims as originally filed. Specifically, support for the amendments can be found in the published application (Publication No. 20050037377) at the following paragraphs:

Support for the recitation of "contacting a sample comprising a binding factor" can be found, for example, at paragraph [0097] and at paragraph [0102] which recites, in part, an "increase in polarization would indicate the presence of at least one binding factor in the **sample** used to bind the probe."

Support for the recitation of "wherein the probe specifically binds to the binding factor forming a binding complex" can be found, for example, at paragraph [0109], [0189] and [0245] which recites, in part, a "fluorescent BPDE-90 mer probe was further used to screen for **specific** binding proteins..."

Support for the recitation of "elecytrokinetic chromatography" can be found, for example, at paragraph [0078] and at paragraph [0156] which recites, in part, the "**electrophoretic** mobility and fluorescence polarization of the fluorescent probe upon complex formation with the binding partner were measured..."

Support for the recitation of "unbound" probe can be found, for example, at paragraph [0072] which recites, in part, the "affinity complexes are readily distinguished from the **unbound** molecules on the basis of their fluorescence polarization..."

Support for "determining the laser-induced fluorescence polarization" can be found, for example, at paragraph [0072] which recites, in part, [T]his invention is directed to a simple method based on **laser-induced fluorescence polarization** (LIFP) detection of an affinity complex of a fluorescent probe and its binding factor."

Support for "exhibits increased polarization in comparison to unbound probe" can be found, for example, at paragraph [0099] which recites, in part, "fluorescence polarization is used to distinguish between a fluorescently-labeled probe and a complex containing both the probe and a factor which binds the probe. The complex exhibits **higher polarization** than the probe...".

No new matter is believed to have been introduced. Claims 1, 2, 3, 4, 11, 12, 16 and 24 are pending and at issue. Applicants request reconsideration of the pending claims.

INFORMATION DISCLOSURE STATEMENT

A copy of the Form 1449 filed in the parent application (US Patent Application Serial No. 09/946,829) accompanies the present Reply.

I. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-4, 11-12 and 15-16 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection as it may apply to the amended claims.

The Office Action alleges that the specification fails to adequately describe "the claimed method for the group of factors as a chemical compound library, specifically a combinatorial chemical compound library." Applicants submit that the claimed method encompasses the use of fluorescence polarization, in combination with electrophoresis, to identify complexes formed when a labeled probe specifically binds to a binding factor. Accordingly, the claimed method can be used to detect the presence of any number of different binding factors in a sample. It is unnecessary to provide a laundry list of every possible binding factor, whether or not included in a chemical library, in the specification in order satisfy the written description requirement of section 112, first paragraph for the claimed method. For example, if the claimed method were limited to a binding factor such as a "nucleic acid sequence," would the Applicants then be required to list every DNA and RNA sequence available from the myriad of databases known to the skilled artisan in order to satisfy the written description requirement? Clearly neither the MPEP nor available case law requires such a disclosure.

The standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed" (see MPEP §2163.02 and In re

Gosteli, 872 F.2d 1008, 1012). An analysis of whether a specification provides an adequate written description of a claimed invention requires one to read the complete specification to determine whether the text as a whole conveys the invention. The case law makes clear that patent disclosures are addressed to persons skilled in the art and the examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. This burden has not been met because the Examiner has failed to explain why the skilled artisan would not recognize that any number of different molecules (e.g., polynucleotide, polypeptide, small molecule) could be detected as a "binding factor" by the claimed method. As is described throughout the specification, all that is required is 1) a molecule possessing chemical characteristics conducive with electrophoresis and 2) a molecule detectable by an increase in polarization of a bound probe. These characteristics of the binding factor would clearly be recognized by the skilled artisan after reviewing the complete specification.

The Office Action further alleges that the claims and/or specification fail to recite any other "means of separation except for CE (capillary electrophoresis). Applicants note that claim 1 has been amended to recite, in part, separating the binding complex from unbound probe by "electrokinetic chromatography." Specific support for the recitation of "electrokinetic chromatography" in the specification has been previously identified. In general, electrokinetic chromatography (EKC) describes a family of electrophoresis techniques named after electrokinetic phenomena, which include electroosmosis, electrophoresis, and chromatography. Electrophoresis refers to the migration of charged electrical species when dissolved, or suspended, in an electrolyte through which an electric current is passed. Capillary electrophoresis is a collection of a range of separation techniques which involve the application of high voltages across buffer filled capillaries to achieve separations. The variations include separation based on size and charge differences between analytes (termed Capillary Zone Electrophoresis, CZE, or Free Solution CE, FSCE), separation of neutral compounds using surfactant micelles (Micellar electrokinetic capillary chromatography, MECC or sometimes referred to as MEKC) sieving of solutes through a gel network (Capillary Gel Electrophoresis, GCE), and separation

of zwitterionic solutes within a pH gradient (Capillary Isoelectric Focusing, CIEF). Capillary electrochromatography (CEC) is an associated electrokinetic separation technique which involves applying voltages across capillaries filled with silica gel stationary phases. Separation selectivity in CEC is a combination of both electrophoretic and chromatographic processes.

The Examiner appears to believe that the pending claims should be limited to the exemplary electrokinetic chromatography technique utilized in the Examples section of the instant specification (i.e., capillary electrophoresis). As generally described above, and as set forth in the specification (e.g., at paragraph [0078] of the published application) the term "electrokinetic chromatography" describes a family of electrophoresis techniques each of which can be used in the claimed method as the mechanism for separating complexes from unbound probe. It is unnecessary for the claims to recite every possible separation technique associated with electrokinetic chromatography. It is also unnecessary for the specification to provide multiple examples utilizing each and every electrokinetic chromatography technique in the claimed method to separate molecules. The specification and claims of a patent application are not required to be "cook books" reciting detailed instructions for practicing the claimed methods such that any reader could practice them. Instead, patent disclosures need only provide information sufficient to apprise the skilled artisan that the Applicants were in possession of the invention defined by the claims. The present disclosure clearly provides the skilled artisan with such information.

In view of the above discussion and in light of the claim amendments, Applicants request that all rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

II. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-4, 11-12 and 15-16 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants traverse this rejection as it may apply to the amended claims.

Applicants note that claim 1 has been amended to recite, in part, the step of "separating the binding complex from unbound probe by electrokinetic

chromatography." This step is entirely self-explanatory and does not require further clarification. Applicants further note that the term "group" has been deleted from the pending claims.

In view of the above discussion and in light of the claim amendments, Applicants request that all rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

III. REJECTION UNDER 35 U.S.C. §102(b)

Claims 1, 3-4, 11-12, 16 and 24 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Laing et al. Applicants traverse this rejection as it may apply to the amended claims.

Applicants note that the pending claims have been amended to recite, in part, a method for: 1) contacting a sample comprising a binding factor with a probe comprising a fluorophore; 2) separating the binding complex from unbound probe by electrokinetic chromatography; and 3) determining the laser-induced fluorescence polarization of the binding complex and the unbound probe. Applicants submit that Laing et al., fails to teach each element of the pending claims and therefore fails to anticipate the claims. Accordingly, Applicants respectfully requests that this rejection be withdrawn.

IV. REJECTION UNDER 35 U.S.C. §103

Claims 1, 3-4, 11-12, 16 and 24 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Laing et al., in view of Rothschild. Applicants traverse this rejection as it may apply to the amended claims.

Applicants respectfully aver that the rejection is based on improper hindsight analysis. The Office Action has set forth no specific understanding or principle within the knowledge of the skilled artisan that would motivate one with no knowledge of the instant invention to combine the teachings of Laing with that of Rothschild.

When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. The Court of Appeals for the Federal Circuit has restated the general principle that hindsight analysis cannot be a basis for an obviousness rejection:

> The [Patent Office] did not, however, explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination [of references cited]. Instead, the [Patent Office] merely invoked the high level of skill in the field of art. If such a rote invocation could suffice to supply a motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. Instead, in complex scientific fields, the [Patent Office] could routinely identify the prior art elements in an application, invoke the lofty level of skill, and rest its case for rejection. To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness. In re Rouffet, 149 F.3d 1350; 47 U.S.P.Q.2D (BNA) 1453, 1458 (Fed. Cir. 1998).

The Federal Circuit has identified three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. In re Rouffet, 47 U.S.P.Q.2D at 1458.

In the instant Office Action, the Patent Office did not sufficiently explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination of Laing with that of Rothschild. The Patent Office alleged that it would have been prima facie obvious to one having ordinary skill in the art at the time of the invention to combine "fluorescence polarization" taught by Laing with the use of "capillary electrophoresis" as taught by Rothschild. It was further alleged that an ordinary practitioner would have been motivated to combine the references because they would "recognize the benefits derived therein" in order to arrive at the claimed method.

The method of Laing is directed to identifying conformational changes in RNA. The method allegedly detects the conformational change in a target RNA sequence when the hybridization of a fluorescently labeled probe is inhibited or modified through the interactions of a ligand with the target RNA sequence. The method of Rothschild is directed to modifying a nascent protein by introducing an amino acid containing a C-terminal marker in to the nascent protein. The C-terminal marker is subsequently used to identify/isolate any protein so labeled. Rothschild cites capillary electrophoresis as one exemplary method of identifying the labeled protein.

Neither Laing or Rothschild suggest detecting a target binding factor by using a labeled probe to form a complex distinguishable from unbound probe through the combination of electrokinetic chromatography and fluorescence polarization. The Patent Office has cited no reference that expressly teaches or suggests such a combination to identify binding complexes. Thus, the Patent Office appears to rely solely on the knowledge of the skilled artisan to provide the motivation to combine electrokinetic chromatography with fluorescence polarization to permit detection of a binding complex. This general motivation is not a sufficient explanation of what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested combining the cited references. Analogous to In re Rouffet, if general motivations or the general state of the art could supply the requisite specific motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. Instead, in complex scientific fields, the Patent Office could routinely place disparate pieces of prior art together to encompass all the elements of a claimed invention to set forth a case for an obviousness rejection. To counter this potential weakness in making obviousness rejections, the "suggestion to combine" requirement stands as a critical safeguard against hindsight analysis. It is improper to conclude that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time of the invention. Fromson v. Advance Offset Plate, Inc., 755 F.2d 1549, 1556, 225 USPQ 26, 31 (Fed. Cir. 1985).

In view of the amendments to the claims, and in light of the above discussion, it is submitted that the skilled person would clearly not arrive at the claimed methods by combining the teaching of Liang with the disclosure of Rothschild. Applicants submit that the claims are patentably distinguishable over the cited references and respectfully request withdrawal of the rejection under 35 U.S.C. §103.

In summary, for the reasons set forth herein, Applicants maintain that claims 1-4, 11, 12, 16 and 24 clearly and patentably define the invention. Applicants request that the Examiner reconsider and withdraw the various grounds for rejection set forth in the Office Action.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (703) 836-6620. No fees are believed due. Should any fees be required, the Commissioner is authorized to charge deficiencies or credit any overpayment to Deposit Account No. 02-4800.

Respectfully submitted,

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